NON-TECHNICAL ABSTRACT

Over the past several years, autologous stem cell transplantation has been used to treat many types of malignancies, including multiple myeloma, chronic myelogenous leukemia, and breast cancer. In this procedure, the patient is treated with standard chemotherapy until the tumor is in the best remission possible. Bone marrow and/or peripheral blood cells are collected and stored. The patient can then receive very intensive drug and radiation treatments aimed at destroying any remaining tumor. The patient's bone marrow function is also destroyed, but the previously collected bone marrow and/or peripheral blood cells can be infused back into the patient to "rescue" him or her and reconstitute bone marrow function. This procedure has been very promising, but a number of questions remain about the best way to perform it. It is not known if the transplanted cells simply provide a "bridge" of bone marrow function until stem cells remaining in the patient recover from the high-dose therapy. Treatment approaches to these three diseases are in development that involve the introduction of new genes into bone marrow or peripheral blood cells to help the patient overcome the tumor, but for these treatments to work, the transplanted cells must survive in the patient for long periods. It is also unclear if tumor cells contaminating the harvested bone marrow and blood are responsible for relapse after the transplantation procedure.

The aim of this protocol is to obtain information about autologous transplantation and about the feasibility of transferring genes to bone marrow and peripheral blood cells that could help other patients with these diseases in the future. We will use specially designed vectors to carry a marker gene into 30% of the harvested bone marrow and/or peripheral blood cells in patients undergoing autologous transplantation for multiple myeloma, chronic myelogenous leukemia, and breast cancer. The remaining 70% will be stored and frozen without gene marking, and will be enough cells to allow recovery after transplantation even if the gene marked cells are not given back. If marking is successful, it will allow us to trace these cells after transplantation, and learn more about the contribution of these cells to recovery and tumor relapse. It will be very important for future gene therapy treatments to learn if "stem cells", or cells in the marrow and peripheral blood that have the ability to produce daughter cells of all blood lineages for prolonged periods of time survive autologous transplantation and can be marked by this gene transfer technique. Gene marking is the only method currently available to distinguish cells originating from the harvested marrow or peripheral blood cells from cells remaining in the patient and surviving the high-dose therapy.